Complete Summary

GUIDELINE TITLE

United Kingdom national guideline for the management of anogenital warts, 2007.

BIBLIOGRAPHIC SOURCE(S)

Clinical Effectiveness Group, British Association for Sexual Health and HIV (BASHH). United Kingdom national guideline on the management of anogenital warts. London (UK): British Association for Sexual Health and HIV (BASHH); 2007. 18 p. [52 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously released version: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD). 2002 national guideline for the management of anogenital warts. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. [43 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Anogenital warts

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Infectious Diseases
Obstetrics and Gynecology
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To reduce the number of sexually transmitted infections (STIs) and the complications that can arise in people either presenting with signs and symptoms of an STI, or undergoing investigation for possible infection
- To offer recommendations on the diagnostic tests, treatment regiments, and health promotion principles needed for the effective management of ano-genital warts, covering the management of the initial presentation, as well as how to prevent transmission and future infection

TARGET POPULATION

Patients in the United Kingdom with anogenital warts

Note: The guideline is aimed primarily at people aged 16 years or older (see specific guidelines for those under 16) presenting to health care professionals.

INTERVENTIONS AND PRACTICES CONSIDERED

Assessment/Diagnosis

1. Assessment of clinical features of lesions
    - Naked eye examination
    - Vaginal speculum examination for females
    - Proctoscopy
    - Meatoscopy, urethroscopy as indicated
    - Recording lesions on genital maps
    - Extragenital site examination
2. Classification of warts as to morphology
3. Biopsy under local anaesthetic for histology, plus or minus colposcopy

Management/Treatment

1. Patient counseling and education
2. Further investigations
    - Evaluation for concurrent sexually transmitted infections

    - Investigation of subclinical lesions, when clinically indicated
3. Pharmacotherapy/chemical applications
    - Podophyllin (not recommended for routine use)
    - Podophyllotoxin
    - Trichloroacetic acid
    - Imiquimod
    - Interferon alpha, beta, or gamma: intralesional; systemic; topical (not recommended for routine use)
    - 5-Fluorouracil (not recommended for routine use)
4. Ablation therapy
    - Cryotherapy
    - Surgical/scissor excision
    - Electrosurgery
    - Laser therapy: carbon dioxide laser
5. Combination therapies
    - Podophyllin with cryotherapy
    - Adjunctive interferon and laser therapy
6. No treatment
7. Assessment of current sexual partner
8. Follow-up
9. Special considerations for the following anatomical sites: intravaginal, cervix, urethral meatus, intra-anal
10. Special considerations for pregnant women
11. Cervical cytology screening intervals
12. Treatment of people with impaired cell mediated immunity

MAJOR OUTCOMES CONSIDERED

- Clearance and recurrence rates of anogenital warts
- Adverse effects of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

OVID/Medline was searched for the years 1966-2006 using keywords "human papillomavirus," "genital warts," "epidemiology," "clinical manifestations," "treatment," "management," "laryngeal papillomatosis."

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia: Evidence obtained from meta-analysis of randomised controlled trials
Ib: Evidence obtained from at least one randomised controlled trial
IIa: Evidence obtained from at least one well designed controlled study without randomisation
IIb: Evidence obtained from at least one other type of well designed quasi-experimental study
III: Evidence obtained from well designed non-experimental descriptive studies such as comparative studies, correlation studies, and case control studies
IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

This guideline was compiled by members of the British Association for Sexual Health and HIV (BASHH) Human Papillomavirus (HPV) Special Interest Group without patient input.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading of Recommendations:

A (Evidence Levels Ia, Ib)

- Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

B (Evidence Levels IIa, IIb, III)

- Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.

C (Evidence Level IV)

- Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities.
- Indicates absence of directly applicable studies of good quality.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Levels of evidence (I-IV) and grades of recommendation (A-C) are defined at the end of the "Major Recommendations" field.

Diagnosis

- Naked eye examination in most cases
- If in doubt, or if the lesion is atypical or pigmented, suggesting possible intraepithelial neoplasia, biopsy under local anaesthetic for histology should be performed prior to any therapeutic intervention. This may be aided by the use of a colposcope.

Assessment of Lesions

- Examine the external ano-genital and surrounding skin under good illumination.
- Females, vaginal speculum examination
- Both sexes, proctoscopy may be indicated if history of anal receptive sex, or following clearance of perianal warts. Meatoscopy and proctoscopy should be performed if there is a history of distortion of urine flow or bleeding from the urethra or anus, respectively. Occasionally urethroscopy is indicated for more proximal warts.
- Classify warts as to morphology.
- Recording of lesions on genital maps at each visit is useful, providing a visual record of approximate number, distribution, and response to treatment.
- Extragenital sites (e.g., oral cavity) examined if clinically indicated.

Management

General Advice

- Patients should be given a detailed explanation of their condition with particular emphasis on the long term implications for the health of themselves and their partners. This should be reinforced by giving them clear and accurate written information.
- Although data are conflicting, condoms have been shown to protect against the acquisition of human papillomavirus (HPV) infection and genital warts and may also have a therapeutic effect when both partners are infected, possibly by preventing continued re-exposure to the virus. Considering current data, condom usage may prove beneficial and their use advisable, particularly in new relationships. (**IIb, B**)
- Latex condoms may be weakened if in contact with imiquimod.
- For some patients the psychological impact of warts is the worst aspect of the disease. Where psychological distress is apparent, referral for counselling may be appropriate.
- There are data suggesting that smokers may respond less well to treatment than non-smokers.

Further Investigations

Many patients will have other concurrent sexually transmitted infections (STIs). Therefore, an appropriate screen for STI is recommended.

Subclinical Lesions

Subclinical lesions of the external ano-genital skin are those not seen by the naked eye, but detectable by soaking the skin with 5% acetic acid and examining with magnification (e.g., a colposcope). These lesions are usually asymptomatic, but may cause irritation and inflammation of the skin—for example, atypical balanoposthitis or vulvitis.

Problems associated with the identification of such lesions:

- Many aceto-white lesions are not caused by HPV.
- Histological changes are not specific for HPV infection.
- HPV detection is not routinely available.

Treatment of these has not been shown to:

- Affect the course of disease in patients or their partners.

For the above reasons and the fact that identification may cause unnecessary distress, it is not recommended that these lesions be sought unless there is a clinical indication (**IIb, B**).

Treatment

Treatment choice depends on the morphology, number, and distribution of warts and patient preference. Treatment decisions should be made after discussing the

appropriate options with the patient, taking into account their preference and convenience.

- The evidence base to direct first and second line treatments is not strong.
- All treatments have significant failure and relapse rates.
- Treatment may involve discomfort and local skin reactions. Written information on management of treatment side effects is recommended.
- Soft non-keratinised warts respond well to podophyllin, podophyllotoxin, and trichloroacetic acid.
- Keratinised lesions are better treated with physical ablative methods such as cryotherapy, excision, or electrocautery.
- Imiquimod may be suitable for both keratinised and non-keratinised warts.
- People with a small number of low volume warts, irrespective of type, are best treated with ablative therapy from the outset.
- Podophyllotoxin, for 4 week cycles, and imiquimod for up to 16 weeks are suitable for home treatment by patients. If chosen, the patient should be given a demonstration on lesion finding and treatment application.
- Local anaesthetic creams plus or minus injection with an injectable local anaesthetic (e.g., 2% lignocaine) could be used before ablative therapy to minimize discomfort. Adrenaline-containing anaesthetic should be avoided for lesions on the penis and around the clitoris.
- No treatment is an option at any site and may apply particularly to warts in the vagina and anal canal.
- Practitioners should consider developing a treatment algorithm or protocol. This has been shown to significantly improve clinical outcome.

Treatments Available

Clearance and recurrence rates for individual treatments are shown in table 1 of the original guideline document.

Chemical Applications

<u>Podophyllin</u>

Podophyllin is a non-standardised cytotoxic compound. It has been associated with severe local reactions. Serious systemic adverse events have occurred when used outside guidelines. Podophyllin is licensed for prescription use only. Best practice described in the British National Formulary recommends supervised application in genitourinary medicine clinics or general practice by trained nurses after screening for other STIs. Animal experiments indicate teratogenic and oncogenic properties but evidence of these in humans is lacking.

- 15-25% solution can be carefully applied to lesions, in clinic, once or twice weekly. Wash off 4 hours later (**Ib, A**).

Caution:

- Podophyllin has caused serious systemic side effects if applied in excess. Increased systemic absorption is likely if used internally. Limit application to

10 cm^2 or 0.5 mL for external warts, and less than 2 cm^2 for vaginal warts (**IV, C**).
- The potential oncogenic and teratogenic effects as noted indicate it should be avoided on the cervix and in the anal canal, and in pregnancy (**IV, C**).

In view of the adverse problems associated with podophyllin and its inferior efficacy to podophyllotoxin (**IIa, B**)—greater than 20% clearance in each of the quoted studies in favour of podophyllotoxin—its use in the routine management of ano-genital warts is no longer recommended. This is in keeping with European opinion.

Combination Therapy

Applications of podophyllin in conjunction with cryotherapy is used in the United Kingdom although there are no studies to validate this approach.

Podophyllotoxin

Podophyllotoxin (Warticon and Condyline), a purified extract of podophyllin in the form of a 0.5% solution or 0.15% cream, is suitable for home treatment (**Ib, A**). It is licensed for 4 and 5 week courses respectively and supervision by medical staff is recommended when the lesion area treated is greater than 4 cm^2. Podophyllotoxin has a license for the treatment of genital warts but not extragenital lesions such as anal warts.

- Treatment cycles consist of twice daily application for 3 days, followed by 4 days' rest for 4-5 cycles.
- The cream may be easier for many patients to apply, especially at the anus.
- Discontinue treatment if significant side effects (e.g., soreness, ulceration).
- Unprotected sexual contact should be avoided soon after application because of a possible irritant effect on the partner.

Caution: Avoid in pregnancy.

Trichloroacetic Acid

Trichloroacetic acid (TCA) 80-90% solution is suitable for weekly application in a specialist clinic setting only. It acts as a caustic agent resulting in cellular necrosis (**Ib, A**).

- An intense burning sensation may be experienced for 5-10 minutes after application.
- Ulceration penetrating into the dermis may occur, and it is therefore not recommended for large volume warts.
- TCA can be used at most anatomical sites.

Caution: TCA is extremely corrosive to the skin. Careful application and protection of the surrounding skin with petroleum jelly is recommended. A neutralizing agent, for example sodium bicarbonate, should always be available in case of excess application or spills.

5-Fluorouracil

5-Fluorouracil is a DNA anti-metabolite, available in a 5% cream. Its use is limited by severe local side effects, which may result in long term problems—for example, neovascularisation and vulval burning. It may be teratogenic and therefore should not be used in pregnancy.

As satisfactory alternatives exist, this treatment is no longer recommended for the routine management of ano-genital warts. (**IV, C**)

Interferons

Various regimens have been described using interferons alpha, beta, and gamma as creams and as intra-lesional or systemic injection (**Ib, A**).

- Its use is limited by expense, systemic side effects, and a variable response rate.
- Cyclical low dose injection used as an adjunct to laser therapy has resulted in a lower relapse rate.
- Interferons are not recommended for routine management of ano-genital warts and should only be used on expert advice (**IV, C**).

Imiquimod

Imiquimod is an immune response modifier.

- Available as a 5% cream, it induces a cytokine response when applied to skin infected with HPV.
- Suitable for use on all external ano-genital warts, but is not recommended for use in pregnancy or internally (**Ib, A**).
- Use in uncircumcised men has been shown to be safe.
- Cream is applied to lesions three times weekly and washed off 6-10 hours later for up to 16 weeks.
- Response to treatment may be delayed for some weeks.
- Clinical trials of imiquimod versus placebo have shown response rates comparable with other chemical agents (**Ib, A**). An apparently low relapse rate has not been compared in clinical trials against other currently available therapies.
- Recent studies suggest fewer recurrences in patients using Imiquimod pre or post surgical excision of lesions.
- Unprotected sexual contact should be avoided soon after application because of a possible irritant effect on the partner.
- Latex condoms may be weakened if in contact with imiquimod.

Caution: Not approved for use in pregnancy or internally.

Physical Ablation

Excision (**Ib, A**)

- Removal of warts under local anaesthetic injection is particularly useful for pedunculated warts and small numbers of keratinised ones at anatomically accessible sites. The use of an anaesthetic cream (e.g., EMLA®) prior to injection is recommended.
- Haemostasis can be established using electrosurgery, silver nitrate, or application of a haemostatic solution.
- Treatment can be repeated as required. This is a good method of treatment for small numbers of warts and may be underused.

Cryotherapy (**Ib, A**)

- Using a liquid nitrogen spray or a cryoprobe results in cytolysis at the dermal epidermal junction resulting in necrosis.
- Treatment should be applied until a "halo" of freezing has been established a few millimeters round the treated lesion.
- A freeze, thaw, freeze technique should be used and lesions held frozen for 10-30 seconds, depending upon size.
- There are health and safety issues to be considered when storing and handling liquid nitrogen. Information and guidance may be obtained from the following sites: British Oxygen (www.bocindustrial.co.uk) COSHH essentials (www.coshh-essentials.org.uk), and the Health & Safety Executive (www.hse.gov.uk).

Electrosurgery (**Ib, A**)

Three types are commonly used:

- Electrocautery results in burning of the treatment site and surrounding tissue.
- Hyfrecator acts by electrofulguration resulting in superficial charring and little dermal damage, or for deeper tissue penetration electro desiccation. These can be followed by curettage.
- Monopolar surgery--different waveforms can be generated, allowing desiccation, cutting, or coagulation. This results in a cleaner cut and less damage to surrounding tissue.

Caution: leave skin bridges between treatment sites to aid healing and minimise scarring.

Laser Treatment (**IIa, B**)

- The carbon dioxide laser is especially suitable for large volume warts and can be used at difficult anatomical sites, such as the urethral meatus or anal canal.

Caution: All electrosurgical and laser techniques result in a plume of smoke which has been shown to contain HPV DNA, which may potentially cause infection of the respiratory tract in operating personnel. Therefore, masks should be worn and adequate extraction provided during these procedures (**IIb, B**).

Sexual Partners

- Current sexual partner(s) may benefit from assessment, as they may have undetected genital warts, undetected other STI, or need an explanation and advice about disease process in partner (**III, B**).
- Tracing of previous sexual partner(s) is not recommended.

Follow-up

- Review is recommended at end of course to monitor response and assess need for changes in therapy. Patients frequently overestimate their response to treatment. Patients whose original lesions have responded well to treatment but new lesions are developing, can continue with current regimen.
- Change is indicated if (a) patient is not tolerating current treatment, (b) under 50% response to current treatment by six weeks (8-12 weeks for imiquimod) (**IV, C**).
- Relapses should be treated as appropriate to the lesion types.

Special Considerations

Anatomical Sites

Podophyllin and 5-fluorouracil are no longer recommended for internal lesions.

Intravaginal

- Cryotherapy, electrosurgery, and TCA are recommended treatments.
- If podophyllin is used it should be applied carefully to no more than a total area of 2 cm^2 weekly.

Cervix

- Cervical intraepithelial neoplasia (CIN) has been documented in patients with cervical warts and for this reason some practitioners have recommended colposcopic assessment and biopsy. The natural history of CIN may be different in women with cervical warts but no study data are available to support this. In keeping with the National Health Service (NHS) Cervical Screening Programme, colposcopy is not recommended in women with genital warts, including those with cervical lesions, unless there is diagnostic uncertainty or clinical concern.
- The following are appropriate treatment modalities for cervical warts: cryotherapy, electrosurgery, TCA, laser ablation, or excision.

Urethral Meatus

- If base of lesions seen, treatment with cryotherapy, electrosurgery, podophyllotoxin, or imiquimod. Lesions deeper in the urethra should be surgically ablated under direct vision, which may require referral to a urologist.

Intra-anal

- Treatment options include TCA, cryotherapy, electrosurgery, and laser ablation. There have been anecdotal reports of successful use of intra-anal imiquimod.

Pregnancy

- Avoid podophyllin, podophyllotoxin, and 5-fluorouracil because of possible teratogenic effects.
- Imiquimod is not approved for use in pregnancy.
- Treatment aims to minimise the number of lesions present at delivery to reduce the neonatal exposure to virus.
- Potential problems for children are the development of laryngeal papillomatosis and anogenital warts.
- Very rarely a caesarean section is indicated because of obstruction of the vaginal outlet with warts or the presence of gross cervical warts. Caesarean section is not indicated to prevent laryngeal papillomatosis/ano-genital warts in the neonate as both conditions are rare.

Cervical Cytology

- The National Health Service Cervical Screening Programme recommends that no changes are required to screening intervals in women with ano-genital warts.
- Guidelines for the management of abnormal smears have been defined.

Immunosuppressed

- People with impaired cell mediated immunity, for example organ transplant patients or those with human immunodeficiency virus (HIV) infection, are likely to have poor treatment responses, increased relapse rates, and an increased risk of developing ano-genital intraepithelial neoplasia.
- Careful follow up is required in all these patients.

Definitions:

The following rating scheme was used for major management recommendations.

Ia: Evidence obtained from meta-analysis of randomised controlled trials
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C (Evidence Level IV)

- Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities.
- Indicates absence of directly applicable studies of good quality.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is graded and identified for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate diagnosis and management of genital warts for patients in the United Kingdom
- Improved wart clearance
- Decreased recurrence rate

POTENTIAL HARMS

- Anxiety from diagnosis
- Treatment side effects:
    - Podophyllin has potential oncogenic and teratogenic effects.
    - Trichloroacetic acid is extremely corrosive to the skin.
    - Imiquimod is not approved for internal use.
    - Liquid nitrogen has health and safety issues.
    - Electrocautery may cause scarring.

Side effects of each treatment option are presented in the "Major Recommendations" field. Side effects may be minimized when the guideline user follows the cautions provided in the original guideline document.

CONTRAINDICATIONS

CONTRAINDICATIONS

Podophyllin, podophyllotoxin, and 5-fluororuracil are contraindicated in pregnancy because of possible teratogenic effects.

QUALIFYING STATEMENTS

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- The recommendations in this guideline may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgement of the clinician and consideration of individual patient circumstances and available resources.
- All possible care has been undertaken to ensure the publication of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing physician to ensure the accuracy and appropriateness of the medication they prescribe.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Clinical Effectiveness Group, British Association for Sexual Health and HIV (BASHH). United Kingdom national guideline on the management of anogenital warts. London (UK): British Association for Sexual Health and HIV (BASHH); 2007. 18 p. [52 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Aug (revised 2007 Jan)

GUIDELINE DEVELOPER(S)

British Association for Sexual Health and HIV - Medical Specialty Society

SOURCE(S) OF FUNDING

Not stated

GUIDELINE COMMITTEE

British Association for Sexual Health and HIV (BASHH) Human Papillomavirus (HPV) Special Interest Group

Clinical Effectiveness Group (CEG)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

British Association for Sexual Health and HIV (BASHH) Human Papillomavirus (HPV) Special Interest Group: Chris Sonnex (Chair), Addenbrooke's Hospital, Cambridge; H Birley, P Fox, R Gilson, C Lacey, R Lau, C Lowndes, R Maw, M Nathan, D Rowen, K Soldan, S Strauss

Clinical Effectiveness Group (CEG) Members: Dr Keith Radcliffe (Chair); Dr Imtyaz Ahmed-Jushuf; Dr Guy Rooney; Dr David Daniels (National Audit Group); Dr Mark Fitzgerald; Dr Gillian Mccarthy; Dr Neil Lazaro (Royal College of General Practitioners)

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Dr R Maw has acted as an adviser to 3M Pharmaceuticals and Stiefel who have sponsored his attendance at scientific meetings. He has also conducted clinical trials for 3M and Perstorp. Dr Fox has received sponsorship to attend scientific meetings and has participated in research sponsored by 3M Pharmaceuticals. Dr

Nathan has conducted clinical trials for 3M Pharmaceuticals and has received sponsorship for attendance at scientific meetings. Dr D. Rowen has conducted clinical trials for 3M and Steifel. Dr Sonnex has conducted clinical trials for Stiefel and acted as an adviser to 3M pharmaceuticals. Dr Lacey has conducted clinical trials for Stiefel and acted as an adviser to 3M pharmaceuticals. Dr Gilson has conducted clinical trials for Stiefel.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously released version: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD). 2002 national guideline for the management of anogenital warts. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. [43 references]

GUIDELINE AVAILABILITY

Electronic copies: Available from the British Association for Sexual Health and HIV Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- UK national guidelines on sexually transmitted infections and closely related conditions. Introduction. Sex Transm Infect 1999 Aug;75(Suppl 1):S2-3.
- Revised UK national guidelines on sexually transmitted infections and closely related conditions 2002. Sex Transm Infect 2002;78:81-2

Print copies: For further information, please contact the journal publisher, BMJ Publishing Group.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on December 8, 2000. The information was verified by the guideline developer on January 12, 2001. This summary was updated on August 5, 2002. This NGC summary was updated by ECRI Institute on December 13, 2007. The updated information was verified by the guideline developer on February 7, 2008.

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